REMARKS

The is a supplement to the response filed on August in response to the Office Action dated November 12, 2004 regarding the above identified application. In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Status of the Claims

Claims 1-4, 9 and 12-14, 16-22, 25-27, and 29-31 are under consideration in this application. Claims 10-11, 15, 23-24 and 28 are being cancelled without prejudice or disclaimer. Claims 1, 13, 16-18, 26, and 29-31 are being amended, as set forth above and in the claim amendments, in order to more particularly define and distinctly claim Applicants' invention.

The claims are being amended to correct formal errors and/or to better disclose or describe the features of the present invention as claimed. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

Informality Rejection

Claims 13-31 were objected to for minor errors. Claims 17 and 30 were rejected under 35 U.S.C. § 112, first paragraph, as introducing new matter by the recitation of "a distance between one of said islands and one of the heat circuits is 10 – 500 μm." Claims 13-15, 26-28 and 31 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

The recitation of "a distance between one of said islands and one of the heat circuits is 10 – 500 μm" is being amended into "a distance between one of said islands and one of the heat sinks is 10 – 500 μm" as supported by page 8, 3rd full paragraph. As the claims are being amended as required by the Examiner, the withdrawal of the outstanding informality rejection is in order, and is therefore respectfully solicited.

Double Patenting Rejection

The non-statutory, obviousness-type double patenting rejection was maintained against claims 1-8 as being unpatentable over claims 1-3 of the patent issued into U.S. Pat. No. 6,428,749 in view of U.S. Patent No. 5,789,167 to Konard (hereinafter "Konard") due to the recitation of "filled with a heat insulating material" not being supported by the specification.

Applicants contend that claim 1 of the application now recites a distinctive limitation of "a heat draining layer shaped in a mesh provided on one side of said first membrane;" that is absent from claim 1 of the '749 patent. Accordingly, the withdrawal of the outstanding double patenting rejection is in order, and is therefore respectfully solicited.

Prior Art Rejections

Claims 1, 13-14, 18, 26-27 and 31 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,093,370 to Yasuda et al (hereinafter "Yasuda"), and against claims 4 and 21 by Yasuda as defined by Giancoli and Handbook of Chemistry & Physics. Claims 6-7 and 9-12 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 6,106,784 to Lund et al. (hereinafter "Lund") in view of U.S. Patent No. 5,789,167 to Konard (hereinafter "Konard"). Claims 2-3, 9-12, 15-17, 19-20, 22-25 and 28-30 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Yasuda in view of U.S. Patent No. 6,051,380 to Sosnowski et al. (hereinafter "Sosnowski"). These rejections have been carefully considered, but are most respectfully traversed.

The biochemical reaction detection apparatus (e.g. Fig. 2B; page 26, 2nd-3rd paragraphs) of the invention as now recited in claim 1, comprises: a first membrane 22 <u>of no more than 20 μm thick</u> (p. 5, 2nd paragraph); <u>a heat draining layer 41 shaped in a mesh provided on one side of said first membrane 22</u> (Figs. 4-5; p. 27, last paragraph); <u>a plurality of islands 21 provided on said one side of said first membrane 21, each space of the mesh 41 having at least one of said plurality of islands being formed therein</u>; probe cells for immobilizing probes for detecting biochemical reactions, each of said probe cells being provided on the side opposite of said first membrane 22 corresponding to one of the islands 21 <u>directly</u> through a cross section of the first membrane 22; and ; and a cover 27 placed on top of the probe cells for accommodating a sample solution layer 26 between the cover 27 and said side opposite to said one side of said first membrane 22 covering all of the probe cells (Fig. 2B; "*Sample solution 26 is preferably added in the amount sufficient for making the solution layer with a thickness of 10-100*

μm After addition of sample solution 26, a glass cover 27 is placed thereon" p. 13, last line to p. 14, 1st line; p. 26, last two lines; Example 5: pp. 36-40). The islands are spaced from each other (page 6, line 15) with intervals, and each of the islands includes a temperature controller for heating and temperature-controlling a corresponding one of said probe cells independently so that the temperature of the sample solution is controlled independently cell by cell (e.g., page 6, line 17; e.g., Fig. 13; "*evaluating 1 kind of sample DNA using 8-base probes*" p. 39, lines 2-3).

According to the present invention, the first membrane 22 is made no more than 20 μm thick by using the mesh-shaped thermal conductor layer 41 to strengthen the first membrane 22. The heat generated at each island readily transmits to the probe cell across the thin first membrane 22, meanwhile the thin first membrane 22 hardly transmits heat sideway to the adjacent probe cells since the mesh-shaped thermal conductor layer 41 drains away such heat. In other words, the thin first membrane 22 provides a very effective path for transmitting heat to the probe cell across the thin first membrane 22, while the mesh-shaped thermal conductor layer 41 prevents heat to transmit to the adjacent probe cells. Hence, each island 21 can control the temperature of each probe cell across the first membrane 22 with high accuracy such that the temperature of the sample solution layer contacted with each probe cell can be controlled independently probe cell by probe cell. For example, a DNA chip in Fig. 13 having 36 probe cells, comprising 4 kinds of probes (probe 2 through probe 5) immobilized on 9 probe cells per each kind of probes. A sample solution is injected onto this chip for hybridization. The temperature for hybridization is set within the range of 10-50°C for each column at intervals of 5°C for the probe cells arranged forming column a through column i (10°C for column a, 15°C for column b, 20°C for column c, . . . 45°C for column h, 50°C for column i). p. 37, 3rd paragraph.

The invention is also directed to a biochemical reaction detection apparatus, as now recited in claim 18, comprising: a first membrane of no more than 20 μm thick, a first side thereof being provided with a sample solution layer; a heat draining layer shaped in a mesh provided on a second side of said first membrane opposite to the first side of said first membrane; a plurality of islands provided on said second side of said first membrane, each space of the mesh having at least one of said plurality of islands being formed therein; and probe cells for immobilizing probes for detecting biochemical reactions, each of said probe cells being provided on the first side of said first membrane corresponding to one of the islands directly through a cross section of said first membrane, each of said

probe cells being set to contact with said sample solution layer. The islands are spaced from each other with intervals filled with air, and each of the islands includes a temperature controller for heating and temperature-controlling a corresponding one of said probe cells independently so that temperature of the sample solution is controlled independently probe cell by probe cell.

The invention is also directed to a biochemical reaction detection apparatus, as now recited in claim 31, comprising all the elements of claim 18 except a first membrane with a first side thereof being set to be provided with a sample solution layer, and reaction products of functional groups not binding with the probes on the first side of said first membrane and polylysine covering said first membrane other than areas provided with said probe cells ("*after the probe is immobilized, the area of the membrane other than that of the probe cell is preferable to be coated with polylysine to make inactive the binding site which is not binding to the probe of the silane coated surface. Polylysine coating can prevent sample DNA, RNA and the like from binding non-specifically with the silane coated surface*" p. 20, 2nd paragraph; "*for reducing the background resulting from the non-specific absorption during the process of hybridization with samples*" p.34, 1st paragraph).

None of the cited prior art references teaches or suggests (1) such "a heat draining layer 41 shaped in a mesh provided on one side of a thin first membrane working in conjunction with the thin first membrane to transmit heat from one island therein across the first membrane to a corresponding probe cell while preventing the heat from transmitting to adjacent probe cells" (claims 1 and 18); or (2) such "reaction products of functional groups not binding with the probes on the first side of said first membrane and polylysine covering said first membrane other than areas provided with said probe cells" (claim 31) thereby controlling "the temperature of the common sample solution being controlled independently probe cell by probe cell." according to the invention.

In contrast, Yasuda's thermal conductor layers among the islands are ***heat sources*** 443 (col. 17, line 39), rather than ***heat drains*** (page 6, lines 1-2 of the outstanding office action), the heat draining layer 41 of the invention. It is well established that a rejection based on cited references having contradictory principles or principles that teach away from the invention is improper.

In addition, Yasuda's heat sources 443 do not shaped into a mesh. As to Yasuda's mesh electrode 753 (p. 10, 4th paragraph of the outstanding office action), it is provided ***within*** each probe cell 7 (Fig. 7; col. 9, lines 5-25), rather than among islands each across said first membrane corresponding to a probe cell, i.e., ***outside*** of each probe cell.

Moreover, there are many elements/layers between the alleged islands and the polynucleotide hybridization area 221 in Yasuda (Fig. 11), rather than directly/only a cross section of the first membrane as in the invention.

Each of the alleged islands in Yasuda (Fig. 11) includes a heating element 225 sandwiched between a planar electrode 226 and one common planer electrode 224 (Fig. 12C) is spaced from each other with intervals filled with a heat conductive (rather than "insulating") material. Since the temperature of a specific target polynucleotide hybridization area 221 is controlled by a potential applied to a pair corresponding electrodes 226, 224 (col. 12, lines 2-11), the material filled between the sandwich structure of 224, 225, 226 must be heat conductive such that the heat evolved by the heating element 225 can be transmitted upward towards a corresponding polynucleotide hybridization area 221, and downwards towards a corresponding thermistor 231 for detecting the temperature of corresponding polynucleotide hybridization area 221 (col. 11, lines 58-62). Inevitably, the sandwich filling material among islands also transmits heat horizontally among different islands. There is simply no mechanism for blocking the heat transmission between adjacent islands in Yasuda.

Several heating element layers 225 are located within one temperature control unit 133, and several thermistors 231 are located within one thermally conductive insulating substrate 132. Specifically, a heating element layer 225 heats the probe hybridization layer 221 through the temperature control unit 133, and this temperature control unit 133 is also in contact with the other heating element layer 225. When the heating element layer 225 evolves heat, the heat is transmitted to the other heating element layer 225 through the temperature control unit 133. Accordingly, temperature of a probe hybridization layer 221 is interfered by that of the adjacent probe hybridization layer 221. Further, the thermistor 231 detects temperature of the probe hybridization layer 221 of interest through the thermally conductive insulating substrate 132. At the same time, it detects temperature of the probe hybridization layer 221 existing in the vicinity. Thus, temperature of each probe hybridization layer 221 cannot be accurately controlled according to the technique of Yasuda.

Sosnowski's SiO2 and Si3N4 layers (col. 24, lines 28-29) was relied upon by the Examiner (p. 9, 2nd paragraph of the outstanding office action) to teach the first membrane of no more than 20 μm thick of the invention. However, they were intended and formed to ***electrically*** "***insulate*** and seal

(col. 25, line 2)" the circuitry, rather than ***conducting heat*** from the island to a corresponding probe cell. Even if, arguendo, a person of ordinary skill were motivated to combine Sosnowski's SiO2 and Si3N4 layers were combined with Yasuda as suggested by the Examiner, such a combined structure would still fall short in fully meeting the Applicants' claimed invention as set forth in claims 1, 18 and 31 since, as discussed, there are no teachings of "(1) such "a heat draining layer 41 shaped in a mesh provided on one side of a thin first membrane working in conjunction with the thin first membrane to transmit heat from one island therein across the first membrane to a corresponding probe cell while preventing the heat from transmitting to adjacent probe cells"; or (2) such "reaction products of functional groups not binding with the probes on the first side of said first membrane and polylysine covering said first membrane other than areas provided with said probe cells" thereby controlling "the temperature of the common sample solution being controlled independently <u>probe cell by probe cell</u>." according to the invention" in either Yasuda or Sosnowski.

The other cited references simply fail to compensate for Yasuda's and Sosnowski's deficiencies. For example. Lund merely concerns a method that does not individually control temperature of each island. Thus, the premise thereof is different from that of the present invention. There is no disclosure of a technical idea for adjusting the interval between islands heated by a temperature controller, etc. or for avoiding the heat transmission between islands.

As such, Yasuda, Sosnowski, Lund, Konard and their combinations fall far short of anticipating or even rendering obvious every feature of the present invention as now claimed in claims 1, 18, 31 and from which claims 2-4 and 9-30 depend. Such differences are more than sufficient that the present invention as now claimed would not have been rendered obvious given the prior art. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

<u>Conclusion</u>

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art reference upon which the rejections in the Office Action rely, Applicants respectfully contend that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of the above-captioned application, the Examiner is invited to contact the Applicants' undersigned representative at the address and phone number indicated below.

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